REMARKS

Claims 1 through 22 were presented for examination in the present application. The instant amendment cancels claims 17 through 19 without prejudice and adds new claims 23 through 26. Thus, claims 1 through 16 and 20 through 26 are presented for consideration upon entry of the instant amendment.

Claims 17 through 19 have been cancelled thus rendering the rejections to these claims moot.

Claims 1 through 22 were rejected under 35 U.S.C. 112, second paragraph. Claims 1 through 16 and 20 through 22 have been amended accordingly. Reconsideration and withdrawal of the rejections to claims 1 through 16 and 20 through 22 are respectfully requested.

Claims 1, 2, 4 through 7, and 13 through 22 were rejected under 35 U.S.C. 102(b) as being anticipated by Casarini et al. (Intl. J. Biochem Cell Biology 2001 Vol. 33, page 75-85) ("Casarini").

Independent claim 1 requires "detecting a presence of the 190, 90, and 65 kDa isoforms, wherein the presence of the 190, 90, and 65 kDa isoforms are used to characterize individuals predisposed for developing hypertension and lesions in characteristic target organs (emphasis added)".

The Office Action asserts "Casarini et al. identify different hypertensive genetic markers, such as 65 kDa, 90 kDa and 190 kDa where the 190 kDa and 65 kDa are in normal individuals, and the maker of 90 kDa appears in hypertension people". See, pg. 4, lines 13-20. Applicants respectfully disagree.

In Casarini, angiotensin I-converting enzyme activity was analyzed in human urine collected from mild hypertensive untreated patients. DEAE-cellulose chromatography was utilized and fractions were pooled and submitted to direct gel filtration in an AcA-34 column and urinary ACES having molecular weights of 90 kDa and 65 kDa were identified; in contrast with the isoforms of 190 and 65 kDa identified in the urine of healthy patients. It was then shown that both forms of ACE bind with all monoclonal antibodies to the active N-domain ACE. Consequently, it was hypothesized that the 90 kDa ACE may have an important role in the development of hypertension. Moreover, the presence of the three isoforms (170, 90, and 65 kDa) were not described in individuals predisposed to develop hypertension.

Thus, Casarini simply does not disclose a method of detecting a predisposition of an individual for developing hypertension and lesions on target organs. In contrast, however, pending claim 1 provides for a direct method of detecting which individuals are likely to develop both hypertensions and lesions on organs. As stated previously, independent claim 1 recites detecting the presence of the 190, 90, and 65 kDa isoforms of ACE and using the presence of these isoforms to characterize individuals predisposed for developing hypertension and lesions in characteristic target organs.

Therefore, Casarini does not disclose or suggest the elements of claim 1. Claim 1 is in condition for allowance. Claims 2, 4 through 7, 13 through 16, and 20 through 22 depend from independent claim 1 and are in condition for allowance for at least the reasons given above for claim 1. Reconsideration and withdrawal of the

rejections to claims 1, 2, 4 through 7, 13 through 16, and 20 through 22 are respectfully requested.

Claim 3 was rejected under 35 U.S.C. 103(a) as being unpatentable over Casarini and further in view of U.S. Patent Publication No. US 20030062475 ("Karst").

Claim 3, which depends from independent claim 1, is in condition for allowance for at least the reasons given above for claim 1.

In addition, the Office Action asserts that "Karst et al. teach that combining both chromatography and mass spectrometer provides advantage of efficient separation of protein complexes from the sample". See, pg. 7, lines 13-17. However, Karst is not prior art to the present application.

Karst has a publication date of April 3, 2003. The present application, however, is a national stage entry filed under 35 U.S.C. 371 of International Application No. PCT/BR2003/000202 filed December 20, 2003, which claims priority to Brazilian Patent Application PI 0206903-2 filed December 20, 2002. Therefore, the present application has a priority date prior to the publication date of Karst. As such, Karst is not prior art.

Claim 3 is in condition for allowance. Reconsideration and withdrawal of the rejection to claim 3 are respectfully requested.

Claims 8 through 12 were rejected under 35 U.S.C. 103(a) as being unpatentable over Hattori et al. Hypertension 2000 Vol. 35, pgs 1284-1290 ("Hattori"). Applicants respectfully disagree.

In Hattori, ACE isoforms were purified and characterized from urine of premature and full-term infants to detect the presence of the N-domain form of ACE. Moreover, 2 peaks of ACE activity from urine of both premature and full-term infants corresponding to the isoforms of 170 kDa e 65 kDa were detected. See, Discussion, pages 1287 and 1288. Nevertheless, the ACE isoforms of 170, 90 and 65 kDa were not considered as hypertensive genetic markers, and neither the 90 kDa isoform was described in the urine of those infants. The only reference in Hattori concerning hypertension is in the abstract which cites that the literature describes that "healthy subjects have high- and low-molecular-weight ACEs (170 and 65 kDa), whereas mildly hypertensive untreated patients have only low-molecular-weight ACEs (90 and 65 kDa), both of which resemble ACE from the N-terminal domain" See, Abstract. Accordingly, the presence of the three isoforms (170, 90 and 65 kDa) in individuals predisposed to develop hypertension were not described.

Thus, Hattori simply does not disclose a method of detecting a predisposition of an individual for developing hypertension and lesions on target organs. In contrast, pending claim 8 provides for a direct method of detecting which individuals are likely to develop both hypertension and lesions on organs.

Therefore, Hattori does not disclose or suggest the elements of claim 8. Claim 8 is in condition for allowance. Claims 9 through 12 depend from independent claim 8 and are in condition for allowance for at least the reasons given above for claim 8. Reconsideration and withdrawal of the rejections to claims 8 through 12 are respectfully requested.

Claims 23 through 26 have been added to point out various

aspects of the present application. Support for new claims 23 through 26 can be found at least in original claims 17 through 19.

It is believed that new claims 23 through 26 are in condition for allowance. For example, new claims 23 through 26 depend from independent claim 1 and are in condition for allowance for at least the reasons given above for claim 1.

In view of the above, it is respectfully submitted that the present application is in condition for allowance. Such action is solicited.

If for any reason the Examiner feels that consultation with Applicants' attorney would be helpful in the advancement of the prosecution, the Examiner is invited to call the telephone number below.

Respectfully submitted,

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